

Remarks

After amendment, claims 1-21 are pending in the present application. Claim 21 is new. Claim 21 is added to provide a slightly different form to originally filed claim 1 and to limit the pH range accordingly. The claims have been amended and new claim 21 has been added to address the Examiner's §112, second paragraph rejection and place the claims in condition for allowance. No amendment has been made to distinguish over the art of record. Support for the amendment to the claims and for new claim 21 can be found throughout the original application and claims and in particular, *inter alia*, on page 4 (first several lines). No new matter has been added by way of this amendment to place this application in condition for allowance.

The Examiner has withdrawn various objection/rejections to the present application but has maintained two rejections: the rejection of the claims under 35 U.S.C. §112, second paragraph and the rejection of the claims under 35 U.S.C. §102(b). For the reasons which are set forth in detail herein, it is respectfully submitted that the claims are sufficiently definite to meet the requirements of 35 U.S.C. and the present claims are patentable over the prior cited against the instant invention. It is respectfully submitted that the claims are now in condition for allowance and the Examiner is respectfully requested to withdraw the current rejections.

The §112, Second Paragraph Rejection

The Examiner has maintained his rejection of claims 1-20 under 35 U.S.C. §112, second paragraph for the reasons which are set forth in the advisory action on pages 2-3. In particular, the Examiner maintains his contention that the use of the term "stabilized" renders the claims indefinite. Applicants respectfully traverse the Examiner's rejection.

In the presently pending claims, the term "stability" is used to describe pH (as amended) and such term is consistent with the fact that initial pH of the composition remains relatively constant, i.e., it does not vary significantly. The present claims refer to pH measurements over at least 2 days, with respect to relative constancy of pH at an initial pH of 3.75. The observations

of the inventors for the pH 3.75 solution indicated that for that upper pH limit there was no more than a 0.05 variation (an increase) for a two day period.

Given the clear teachings in the specification of the present application as set forth above, it is respectfully submitted that Applicants' claims particularly point out and distinctly claim the subject matter which Applicants regard as their invention. It is respectfully submitted that claims 1-20 are in compliance with the requirements of 35 U.S.C. §112.

The Rejection of Claims 1-20 Under 35 U.S.C. §102(b)

The Examiner maintains his rejection of previously presented claims 1-20 as being anticipated by the disclosure of Benjamin, et al., US Patent Application Publication US2002/0136750 ("Benjamin, et al.") for the reasons which are set forth in the Advisory Action on page 3. For the reasons which are set forth hereinbelow, Applicants respectfully submit that the present invention is not anticipated by the disclosure of Benjamin, et al. for the simple reason that the reference does not disclose *all* of the claimed elements of the present claimed invention, which is required to make out a cogent rejection based upon anticipation.

The Benjamin Teachings Do Not Disclose Each and Every Element of the Claimed Invention

Benjamin *et al.* have demonstrated in their supportive examples, regarding the introduction of nitrite to the organisms, not *vice versa*, as one would ordinarily apply an active germicide to an organism in a contaminated or infected area. Because of the necessity of having oxides of nitrogen available as the germicide, Bajmain, et al. first mix the bacterium into a buffered inoculum at the desired pH, and then add the sodium nitrite. This is true in their first three Examples. Note that is done because, as is shown in Figure 4 (as referenced in Example 4), this "shows the release of nitric oxide as a result of reducing pH...." (which) "readily diffuses through cell membranes... and damages bacterial DNA." Benjamin's Figure 4 shows that the generation of nitrogen oxides drops precipitously, from the first minute of combination to about four minutes thereafter, irrespective of starting concentration of sodium nitrite. That is why the

mixture and the organism have to be first intimately in contact when the system is prepared. Not so for our system, which represents a decidedly distinguishable advance over the teachings of Benjamin, et al., a low pH maximum (which is significant) and a range of nitrous acid/nitrite ratios which is different.

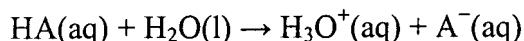
Implicit in Benjamin's Example 5 is that the patients received application of the fresh mixture as soon as it was prepared. There is nothing in the text to indicate otherwise, *i.e.*, the assumption being that the NOxides in the fresh mixture was the intended curative agent.

Note that there is a glaring omission, in Benjamin's Example 6, where they cite "the use of nitrate or nitrite administered topically in the mouth.. to reduce..caries-producing organisms.. and to prevent infection with C albicans.." thereby showing "such application to be effective." Contrary to the Examiner's contention, there is *no indication that an acidified nitrite system was employed*, only that in some manner, because of the presence of just nitrate or nitrite alone, Benjamin states that it **"is possible that Lactobacilli sp. transiently produce sufficient acid in the mouth... to control the growth of oral pathogens..."** It is well documented that saliva, as most other bodily fluids, tries to maintain itself at a near normal pH of about 7. It is highly unlikely that an organism would produce sufficient acidity to trigger NO production, which would require a minimum of 1000-times more H⁺ ions (at a pH of 4 rather than at 7) locally, to effect such triggering. Thus, Benjamin, et al. clearly does not teach the present invention as is contended by the Examiner. First, E Coli was in the acid buffer **before** the nitrite was added (for NO production), and second, there was no acid whatsoever in Benjamin's reference to use as an oral treatment in his Example 6. Thus, Benjamin, et al. cannot be fairly taken to teach or disclose the present invention.

As a further note, regarding support for the arguments that buffer pHs can only rise, the Examiner indicates that "Applicants offer no support for their argument.." that "...pH in buffers only rises rather than decrease " when referring to acidic buffers. An understanding of the basic functioning of buffers, whether acidic or basic, should be sufficient to provide such support. The following discussion regarding buffering systems should provide sufficient support to defuse the Examiner's arguments. It shall hopefully prove to be instructive.

Consider the classical definition of an acidic buffer, *i.e.*:

“Acidic buffer solutions are solutions which resist change in hydrogen ion concentration (and consequently pH) upon addition of small amounts of base, or upon dilution. These buffer solutions consist of a weak acid and its conjugate base. The resistive action is the result of the equilibrium between the weak acid (HA) and its conjugate base (A⁻):”



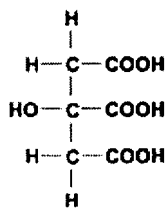
When an acid, HA, dissolves in water, some molecules of the acid dissociate to form the H₃O⁺ hydronium ions and the conjugate base, A⁻ of the acid. The acid dissociation constant is defined as

$$K_a = \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]}$$

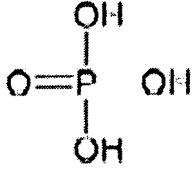
where the square brackets are usually taken to signify concentration. The pK_a, the negative logarithm of the acid dissociation constant, is taken as:

$$\text{p}K_a = -\log_{10} K_a$$

Consider a weak acid, such as the α-hydroxy acid lactic acid, to illustrate the principle. [This is an acid with a single hydroxyl function, in the same family as the other, multiple-carboxy [HA] α-hydroxy acid citric acid, or function as the weak acid phosphate system, referenced by the Examiner in his citation of the Xu *et al.* citrate-phosphate buffer on Page 4 of his earlier rejection (08/30/2006)]. The same principle will apply to all incompletely ionized acids, whether citric acid or phosphoric acid, which form ionization pairs in the pH relevant range of this application, *i.e.* <pH 4.0. For citric acid, that would be:

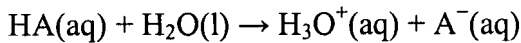


, and its corresponding monosodium salt, where one of the -COOH moieties is replaced by -COO⁻ Na⁺, for which a pK_a value of 3.13 is characteristic. That figure represents the pH of a solution in which equimolar amounts of unionized and singly ionized monosodium citrate exist in solution. Or for phosphoric acid,



, and its corresponding monosodium salt $[\text{OH}]_2\text{P}=\text{O} [\text{O}^- \text{Na}^+]$, for which a pKa of 2.15 is characteristic (the pH of the aqueous solution at which equimolar amounts of H_3PO_3 and $\text{H}_3\text{PO}_2^- \text{Na}^+$ exist).

Consider again the nature of an acidic buffer system:



Upon the addition of an alkaline material to this acidic buffering system, which is initially at a pH within the capability of the solution to maintain a pH approximating that of its pKa value, a portion of the hydronium ion, H_3O^+ , is neutralized. This causes some of the HA to further dissociate, driven by chemical forces to maintain the equilibrium defined by its acid dissociation constant. This results in an increased pH for the system, as defined by the well-known Henderson-Hasselbalch equation. That equation (see below) derives directly from the above expression, by rearranging the expression defining the dissociation constant, and putting $\text{pH} = -\log_{10}[\text{H}^+]$.

$$\text{pH} = \text{pK}_a - \log \frac{[\text{HA}]}{[\text{A}^-]}$$

Assume a range of dissociation of the acid from 1% to 99% dissociation. It can be deduced from this expression that

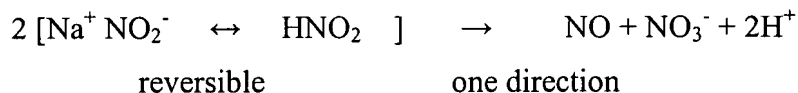
- when the acid is 1% dissociated, that is, when $\frac{[\text{HA}]}{[\text{A}^-]} = 100$, $\text{pH} = \text{pK}_a - 2$

- when the acid is 50% dissociated, that is, when $\frac{[\text{HA}]}{[\text{A}^-]} = 1$, $\text{pH} = \text{pK}_a$

- when the acid is 99% dissociated, that is, when $\frac{[\text{HA}]}{[\text{A}^-]} = 0.01$, $\text{pH} = \text{pK}_a + 2$

It follows that the range of pH within which there is partial dissociation of the acid (*e.g.* from 1% to 99%) is about $pK_a \pm 2$. And as the unionized acid becomes more and more ionized, following consumption of the H^+ (as the H_3O^+ hydronium ion), *e.g.* as a buffer is being depleted, the pH of the solution will consistently *rise*. If a citrate buffer, for example, was set at its 3.13 pKa value, where 50% of the first carboxylic acid was dissociated, then as more and more of it was neutralized, when acting in its buffering capacity, the pH of the solution would rise to 5.13 as its buffering capacity was being exhausted. There is never a situation where a buffer solution, when absorbing the neutralizing influences of exogenous alkaline substances, *will decrease in pH*. Such a contention flies completely against conventional chemical understanding.

There can only be a pH drop when additional acidity is being added to the system, externally or endogenously. The latter occurs in the chemistry of the pending application, as the system itself generates additional H^+ ions through a non-reversible and ongoing disproportionation reaction. This is the situation for the continued progression of the nitrous acid degradation, where the HNO_2 molecule is formed from nitrite ion and H^+ ions provided by continued dissociation of



As nitrous acid degrades, over the extended course of the system (which has been shown in our application to be ≥ 2 years), the continuous production of H^+ ions in solution continually drives the pH to lower levels. The inventive composition can attain a pH value as low as around pH 2.5 over a period of about two to five days, and the degree to which it drops is determined by the initial pH of the combined nitrite/acid system. At an initial pH of about 3.7, there is little change in pH upon standing, and approximately stabilizes at that pH value as is claimed. The further below that figure the initial pH is, the more significantly the pH decreases relative to that initial pH. This is evident in the data provided on page 9 of the pending application, for solutions aged for 30 days, *viz.*

<u>pH at T=0</u>	<u>pH at T=30 days</u>
2.94	2.30
3.12	2.50
3.35	3.25
3.54	3.15
3.75	3.92
3.90	4.35

What should be inferred from these data is that the greater the initial concentration of nitrous acid, in equilibrium with nitrite ion in solution, the greater the drive for its disproportionation, according to the equation:



The evaporation of the NO gas from the system has no impact on the kinetics of the system, and the inventors have shown that, despite the cited prior art by Benjamin *et al.*, the system retains a high level of germicidal activity. This is counter to the Examiner's previous argument that the "prior art compositions are expected to show such functional properties because they are deemed to be the same compositions comprising same ingredients." As previously argued, Benjamin *et al.* specifically require the presence of nitrogen oxides for their system to function, and dictate the separation of the components of their final composition so that, once formed, such oxides will exert their effects. It is evident, throughout the application, that these compositions lose their efficacy a short time after combination. In these inventive compositions, by defining the molar percentages of nitrite as nitrous acid *ab initio* (about 35% but less than about 95%) within the much broader range of nitrite and acid concentrations cited by Benjamin *et al.*, the inventors teach how such acidified nitrite systems can provide extended activity (up to at least five days and, as shown in the application, to at least 2 years).

All of the Examiner's citations on Page 7, regarding the varied applications of the Benjamin *et al.* compositions (*e.g.*, in cream or lotion form, against *E. coli*, on foot fungal infections, but not as a mouthwash *vide supra*) rely on an initial composition which is not representative of the composition of our inventive composition a short while after mixing, after

the NOxides are lost. Consequently, it is respectfully submitted that Benjamin, et al. cannot be seen as anticipating the present invention.

It is respectfully submitted that the Examiner has not made out a cogent case that the present invention is anticipated by the disclosure of Benjamin, et al.

The Rejection of Claims 10-13 15 and 16-19 Under 35 U.S.C. §103

The Examiner has rejected originally filed claims 1-20 as being unpatentable over Xu, et al., in view of Kross, et al., and further in view of Benjamin, et al. for the reasons which are set forth in the office action on pages 9-12 and as further detailed in the Advisory action on page 4. Essentially it is the Examiner's position that the disclosure of Xu, et al., can be combined with the teachings of Kross, et al., further in view of Benjamin, et al. to provide the present invention. Applicants respectfully traverse the Examiner's rejection.

The stark differences between the presently claimed compositions and the compositions which are disclosed by Xu, et al. have been discussed in great detail in a previous submission. In short, Xu, et al., do not disclose compositions which are even remotely related to the present invention, in that the concentration of nitrite and nitrous acid of Xu, et al. is significantly different than in the present invention and the ratio of nitrous acid to total nitrite in the composition fall within specific percentages, which are markedly distinguishable over the compositions of Xu, et al. which are prepared to mimic compositions in the gastrointestinal tract. There is absolutely no disclosure in Xu, et al. of the present compositions, or the requirement for certain concentrations of a nitrite salt or a relative percentage of nitrous acid to total nitrite salt in the composition which provides a stable composition that exhibits substantial germicidal activity over long periods of time. There is absolutely no suggestion in Xu, et al. of the present invention and there is simply no motivation taught to provide or pursue the instant compositions. The present invention is clearly non-obvious over Xu, et al.

Further to Applicants' arguments made hereinabove, Applicants have additional reasons for the non-obviousness of the present invention. In this regard, Applicants further point out, with respect to the term "stability", as has been defined in great detail hereinabove, the Examiner's objection (see page 10, lines 6-8), with regard to the description that the Xu, et al. compositions evoke stability, in stating that "Even though Xu *et al.* does not report the long term variability of the nitrite solution, it is expected to remain stable because citrate-phosphate is a strong buffer in acidic conditions" (emphasis added). Applicants strongly disagree. The Examiner cites this as analogous to our recitation that "the pH of the composition either remains relatively constant at an initial value of around 3.75 or lower at the time of formulation to a value as low as around 2.5 over a period of at least about two days." It is respectfully submitted that the Examiner has failed to appreciate the major difference in these two situations. As we have previously argued in our last filing [on page 6, 2nd full paragraph, line 8], and which is referenced here "In point of fact, the Examiner's reference to citrate-phosphate buffers remaining pH-stable is inconsistent with ...the changing and decreasing pH values of the inventive compositions.." As has been stated hereinabove, the very nature of buffers, specifically acid buffers as taught by the cited prior art, is to maintain the pH of a system as to resist *alkaline* or pH raising factors, which may otherwise drive the pH higher in the direction of neutrality.....Ultimately, as ... the buffering capacity is consumed, the pH of the system will rise rather than lower as is the case of the presently claimed compositions." This is the exact opposite of the present invention and in this manner actually *teaches away*. Moreover, as the Examiner has previously pointed out, "The buffer solution of Xu *et al.* is considered an "application medium." (See the last line of page 10 of the final office action). As pointed out, the compositions of the present invention are *not* buffer solutions, which are used to counter the influence of basic materials introduced to the solution while depleting its own acidity, but rather *solutions where the pH of the system will tend toward an increasing acidity (lower pH), as the nitrous acid disproportionates to form, inter alia, nitric acid*. Thus, the compositions of Xu, et al. and the present invention are dramatically different compositions working in essentially opposite directions as these compositions relate to pH.

The reason why the pH of the *present* compositions will *lower* as claimed, in contrast to the compositions of the cited art, can be directly traced to the reaction shown on page 9 of the present application, whereby the degradation of three nitrous acid molecules [3HNO_2], through a change of the +3 valence of the N atom, leads to the creation of a solution of nitric acid [$(\text{H}^+) + (\text{NO}_3^-)$]; where the complete ionization of the resulting nitric acid leads to a more-acidic solution than that of the fractionally ionized HNO_2 progenitive species. Again, acid buffer solutions, such as citric-phosphoric compositions, will invariably rise in pH, upon depletion of the H^+ ion, whereas the inventive compositions will decrease in pH by producing H^+ ions. In our case, a chemical reaction, with electronic changes, is the basis for the pH lowering. In acid buffer solutions, it is simply a changing balance between the anion and its corresponding acid form that is responsible for the buffering effect.

With respect to the teachings of Xu, et al., the Examiner points out that “the levels of metal nitrite disclosed in Xu *et al.* is 0.00050%- 0.0050%” and he interprets the upper range of “about” 0.0050% to be included in the “about 0.01 to 1.0 range claimed herein.” As has been previously pointed out, it is respectfully submitted that the **Examiner has made an error here**, which goes to heart of the absence of cogency of the obviousness rejection. In point of fact, Xu *et al.* did not indicate a range of 0.00050% - 0.0050% metal nitrite in their publication. Rather, Xu, et al. cited nitrite concentrations [not metal nitrite] of 0.00033% to 0.0033%. The figures cited by the Examiner are those found on page 12 of our previous filed response of December 22, 2006 where, for the purpose of comparison with the Benjamin levels and Applicants’ levels, both expressed as “metal nitrite”, it was presented what the Xu levels would be, if (hypothetically) similarly expressed as metal nitrite. The term metal nitrite never appears in the Xu paper, nor does Xu indicate what form of nitrite was used in their experiments. Xu, et al., simply mention the addition of “nitrite” at different levels to their media. Consequently, it is Applicants’ respectful submission that the Examiner’s arguments are further negated, when attempts are made to interpret the upper level of Xu’s 0.00033% to 0.0033% nitrite as being included in the present invention’s lower specified metal nitrite concentration of 0.01% in the 0.01% to 1.0% range. ***They are not.*** Moreover, the Examiner further admits that “Xu *et al.* does not expressly disclose the use of metal nitrite to generate nitrous acid...” in connection with a method of disinfection...”over a period of several months.” Consequently, it is Applicants’ position that the

Examiner's two objections, based on Xu *et al.* come down to 1)- a comparison with known buffers (as described hereinabove), which does not apply in the present instance for the reasons cited, and 2)- an overlap of the two ranges 0.00033% to 0.0033%, as nitrite, and 0.01% to 1.0% as metal nitrite, which point in fact, **does not exist**. It is respectfully submitted that Xu, et al. clearly does not render the present invention obvious.

In the advisory action, the Examiner continues to argue "that Xu's nitrite concentration of 0.0033% is still considered to fall within the "about 0.01% range claimed herein." And that someone of ordinary skill in the art would make such an adjustment, when extrapolating a system designed for simulating stomach conditions to a Long-Acting Nitrous Acid composition that can be effective for at least two days, and much longer as well. Applicants believe, however, that a skilled chemical artisan would never stretch so far or to be motivated, as to first use a simulated transient biological process as prior art to practice what is now embodied in the present invention, particularly since the **upper** limit of 0.0033% of the experimental study would lie significantly *below* the **lower** limit of the 0.01 to 1.0 percentage range of the present invention. Xu, et al. simply does not teach or suggest the present invention.

To reiterate, Applicants restate the earlier arguments as follows:

- The Examiner points out that "the levels of metal nitrite disclosed in Xu *et al.* is 0.00050%- 0.0050%" and he interprets the upper range of "about" 0.0050% to be included in the term "about 0.01 to 1.0 range" claimed in the present invention. Applicants respectfully submit that the Examiner has made an error here, which vitiates his argument regarding Xu, et al.. Xu *et al.*, in point of fact, did not indicate a range of 0.00050% - 0.0050% metal nitrite in their publication. Rather, they cited nitrite concentrations [*not metal nitrite*] of 0.00033% to 0.0033%. The figures that the Examiner cited are those found on Page 12 of our earlier reply where, for the purpose of comparison with the Benjamin levels and levels of the present invention, both expressed as "metal nitrite," the present inventors calculated what the Xu levels would be, if similarly expressed as metal nitrite. They are not the same as used in the present invention. Moreover, the term metal nitrite never appears in the Xu paper, nor does Xu indicate what form of nitrite was used in their experiments. Xu, et al., simply mention the addition of "nitrite" at different levels to their media. Thusly, the Examiner's arguments

are further vitiated, when one *attempts to interpret and assign the upper level of Xu's 0.00033% to 0.0033% nitrite as being included in the metal nitrite concentration range (0.01% to 1.0%) of the present invention. The Examiner further admits* [2nd paragraph, page 11] that "Xu *et al.* does not expressly disclose the use of metal nitrite to generate nitrous acid.." in connection with a method of disinfection..."over a period of several months." Therefore, the Examiner's two objections, based on Xu *et al.*, come down to a comparison with known buffers (above paragraph), which does not apply here for the reasons cited, and to an overlap of the two ranges 0.00033% to 0.0033%, as nitrite, and 0.1% to 1.0% as metal nitrite.

It is respectfully submitted that Xu, et al. does not teach or render the present invention obvious.

Turning to Kross, et al, this reference, is perhaps inapposite to the present invention, inasmuch as it teaches certain chlorous acid/chlorite systems for disinfecting meat carcasses. There is absolutely no disclosure in Kross, et al. of a nitrous acid/nitrite system and there is absolutely no suggestion of the present compositions which are based upon nitrous acid/nitrite. Given that Xu, et al. clearly fail to motivate the present compositions, and Kross, et al. are not even related to the same chemical system as in the present invention, it cannot be cogently asserted that the presently claimed compositions are obvious over the disclosure of Xu, et al., in view of Kross, et al. The argument that the Examiner makes that one could take the teachings of Xu, et al., regarding compositions which do not teach the limitations of the present invention or desirability of the chemical characteristics of the present invention and somehow combine that disclosure with Kross, et al., which is directed to a *different chemical system* than the present invention, to produce the presently claimed invention is simply not a cogent argument and should be withdrawn. It is respectfully submitted that the presently claimed invention is clearly non-obvious over the teachings of Xu, et al., in view of Kross, et al.

Benjamin, et al. do nothing to obviate the deficiencies of the Examiner's rejection. As discussed hereinabove, Benjamin, et al. completely failed to appreciate the compositions according to the present invention given the absence of even an oblique reference or teaching directed to stability, given the immediate use of the compositions in Benjamin, et al.

From another perspective, the present inventors have established that the compositions of the present invention are capable of long-term disinfection, long after any nitrogen oxides have dissipated, which is completely contrary to the Benjamin teachings. The Benjamin, et al. compositions, with their nitrogen oxides included, are not the same as those of the present invention, where nitrogen oxides may or may not be present. In a 2-year stored composition of the present invention, that showed activity equal to what was found at T=0, there was no remaining gaseous NOxides. The present inventors achieve that stabilization with metal nitrite compositions within the 0.01-1.0% range- there is absolutely no evidence that the full range of the Benjamin alkali metal compositions [*i.e.*, 0.5% - 30%] would be capable of maintaining germicidal capability, particularly those which fall outside of our stipulated range of HNO₃/NO₂⁻ ratios. Below an initial pH of ~2.0, (95% nitrite ion as nitrous acid), there might be so much NO blown off, that long term stability would not be achievable, and these compositions are included in the Benjamin teachings. Similarly, above a pH of about 3.6 (35% nitrite ion as nitrous acid), the pH of the solution would drift upwards with time, as we have shown, and pHs from 3.6 to 4.0 are included in the Benjamin teachings. Less acidic nitrite solutions have *de minimus* activity. Thus, Benjamin, et al. clearly did not appreciate the present invention.

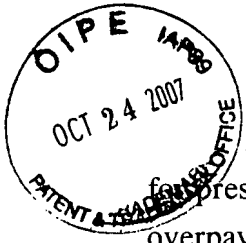
Applicants take issue with the Examiner's comments on page 11, line 4 *et seq.* that "...it is well settled that 'intended use'" prevents the allowability of the claimed invention because "...the prior art discloses the same composition comprising the same composition comprising the same ingredients..." Benjamin *et al.* point out, repeatedly, as Applicants have shown, that the composition that is formed immediately upon the combination and application of the mixture, contains nitric oxide and then other nitrogen oxides, as the germicide. That is the "composition" that is basic to Benjamin, as pointed out, in Benjamin, et al. (see paragraph [0027]) where the ingredients "are separately disposed..for admixture at the intended environment to release NO or NO₂ ions." Thus, the operative composition as taught by Benjamin, et al. is the mixture which contains these oxides. In stark contrast, the present invention is directed to compositions with little or none of the originally formed NOxides as the basis for the long-term germicidal efficacy of stabilized or downward drifting pH solutions of the present invention. Thus, the present invention stands in complete contrast to Benjamin as it relates to the basic composition and its teachings.

Moreover, with respect to the Examiner's argument regarding the teachings by Kross of the use of antimicrobial agents on animal carcasses that "it would be obvious ..to use a metal nitrite in a composition that comprise...well known buffers to make a stabilized composition" in view of the combined teachings of Xu *et al.*, Kross and Benjamin, the point must be made here that the compositions of the present invention are based on a defined small range of metal nitrite concentrations, within the broad range cited by Benjamin *et al.*, wherein the limited concentrations of nitrite exist in a specifically defined ratio of $\text{HNO}_2/\text{NO}_2^-$ {~0.54 to ~ 19 corresponding to the 35% to 95% nitrite as nitrous acid concentrations}.

As a final note, with respect to the obviousness of the present invention over the cited art, it is respectfully submitted that "conventional wisdom" supports the patentability of the present invention inasmuch as Benjamin, et al. supports the view that because of "conventional wisdom" the compounds disclosed therein must be used very soon after mixing and there is no motivation or suggestion to do otherwise. Indeed, one of ordinary skill, relying on conventional wisdom and the teachings of Benjamin, et al., would *not* do otherwise. In contrast, the genesis of the present invention relies on not following the conventional wisdom and instead, creates an invention which stands in complete contrast to the conventional wisdom and the teachings of the art. In fact, Benjamin *et al.* teach that the acid nitrites in the disclosed compositions only work because the NOxides that are generated upon combination quickly *dissipate*, whereas the present invention is directed to compositions where the compositions are active for a much longer time. These are completely different concepts, standing in complete contrast to each other. .

It is respectfully submitted that the present invention is non-obvious over the teachings of Xu, et al, in combination with Kross, et al., further in view of Benjamin, et al.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

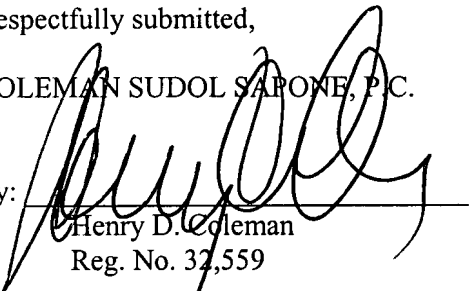


Applicants have added one independent claim. A fee in the amount of \$100 is enclosed for presentation of the additional claim 21. If a determination that any further fee is due or any overpayment is made, please charge/credit Deposit Account No. 04-0838. A Request for Continued Examination and fee, as well as a petition for a one month extension of time is also enclosed.

Should the Examiner wish to discuss the present application in an effort to advance its prosecution, the undersigned attorney may be reached at the telephone number set forth hereinbelow.

Respectfully submitted,

COLEMAN SUDOL SAPONE, P.C.

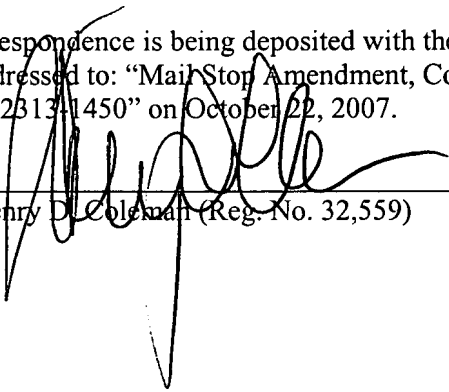
By: 
Henry D. Coleman
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Dated: October 22, 2007

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